

Role of TGF- β Activated Kinase 1(TAK1) in Chick Retinal Development

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Bone morphogenetic proteins (BMPs) play a critical role in vertebrate eye development by regulating cell fate processes in the retina through canonical SMAD and non-canonical MAPK pathways. TGF- β Activated Kinase 1(TAK1) is a MAPKKK that activates the MAPK cascade upon BMP activation. Dysregulation of TAK1 is associated with a variety of diseased states including cancer, but little is known about the role of TAK1 in development. Recent in vitro studies have indicated that TAK1 inhibits the G1-S phase Cyclin D, a process known to be critical to cell cycle exit. Although no studies have focused on the role of TAK1 in retinal development, many studies have indicated that BMPs as well as properly timed cell cycle exit are critical for the differentiation of specific cell types. In studies designed to test the hypothesis that TAK1 is an essential regulator of cell cycle exit in the chick embryonic retina, we have performed immunohistochemistry using an antibody that specifically detects the activated form of TAK1 (pTAK1) and shown the extensive localization of pTAK1 in a subset of differentiated cells and, more prominently, in the mitotic progenitor cells of the retina. Our preliminary studies, aimed at in vivo pharmacological inhibition of TAK1 activity using (5Z)-7-Oxozeaenol in the developing chick eye, show that TAK1 inhibition could lead to a range of developmental defects in the retina. While further studies focusing on molecular changes resulting from TAK1 inhibition and overexpression would shed more light on its functional role in the retina, our results suggest that TAK1 signaling is critical for normal eye development. The heavy localization of pTAK1 in mitotic progenitor cells especially, could be indicative of its role in cell cycle exit. Understanding the functional role of this protein in the context of eye development could aid in understanding the pathophysiology of diseased states associated with TAK1.

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